

Attorney Docket No. 5470-148

PATENTS

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Baldwin, et al.	)	Examiner: T. McKelvey
Serial No.: 08/959,160	)	
Filed: 28 October 1997	)	Art Unit: 1636
For: Use of NF- $\kappa$ B Inhibition in Combination	)	
Therapy for Cancer	)	Date: 8 April 1999

Declaration of Albert S. Baldwin, Jr.

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231



Sir:

I, Albert S. Baldwin, Jr., declare as follows:

1. I am a named co-inventor on US Patent Application Serial No. 08/959,160, filed 28 October 1997 and entitled "Use of NF- $\kappa$ B Inhibition in Combination Therapy for Cancer".

2. The following experiments were carried out with my participation, and were conducted to determine the effects, on colorectal tumors of human origin grown in nude mice, of a proteasome inhibitor of NF- $\kappa$ B and an antineoplastic chemotherapeutic agent.

3. Colorectal tumors of human origin (LOVO tumors) were grown in nude mice to a volume between 0.6 cm<sup>3</sup> and 0.8 cm<sup>3</sup>. The known antineoplastic chemotherapeutic agent irinotecan (CPT 11) was given every five days in combination with a different concentration of the proteasome inhibitor PS-341 (ProScript, Inc., Cambridge, MA). The proteasome inhibitor PS-341 is an inhibitor of NF- $\kappa$ B due to its ability to block the degradation of I $\kappa$ B, which is the inhibitor of NF- $\kappa$ B.

4. Results are shown in Figure 1. As shown, PS-341 at either 1 mg/kg or 2.5 mg/kg, in combination with CPT-11, caused tumor regression.

DECLARATION OF DR. BALDWIN  
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5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Albert S. Baldwin  
Albert S. Baldwin, Jr.

April 8, 1999  
Date



## Response of LOVO Tumors to Combined Treatment with CPT-11 and Increasing Dosage of PS-341

